

(a) X is selected from the group consisting of  $-S(O_2)-$ ,  $-N(R')-S(O)_2$ ,  $S(O)_2-N(R')-$ ,  $-C(=O)-$ ,  $-OC(=O)-$ ,  $-NHC(=O)-$ ,  $-C(=O)N(R')-$ ,  $-P(O)(R')-$  and a direct link, wherein  $R'$  is independently hydrogen, alkyl of 1 to 4 carbon atoms, aryl of 6 to 14 carbon atoms, aralkyl of 7 to 16 carbon atoms, with the proviso that when X is  $-P(O)(R')-$ , the  $R'$  is not hydrogen;

(b)  $R_1$  is selected from the group consisting of:

(1) alkyl of 1 to 12 carbon atoms which is optionally substituted with  $Y_1$  and/or  $Y_2$ ,

(2) alkyl of 1 to 6 carbon atoms substituted with cycloalkyl of 3 to 8 carbon atoms which is optionally mono-, di-, or tri-substituted with  $Y_1$ ,  $Y_2$  and/or  $Y_3$ ,

(3) cycloalkyl of 3 to 15 carbon atoms, which is optionally mono-, di-, or tri-substituted on the ring with  $Y_1$ ,  $Y_2$  and/or  $Y_3$ ,

(4) heterocycloalkyl of 4 to 10 ring atoms with the ring atoms selected from carbon and heteroatoms, wherein the heteroatoms are selected from the group consisting of oxygen, nitrogen, and  $S(O)_i$ , wherein  $i$  is 0, 1 or 2, which is optionally mono-, di-, or tri-substituted on the ring with  $Y_1$ ,  $Y_2$  and/or  $Y_3$ ,

(5) heterocyclo of 4 to 10 ring atoms with the ring atoms selected from carbon and heteroatoms, wherein the

heteroatoms are selected from the group consisting of oxygen, nitrogen, and S(O)<sub>1</sub>, which is optionally mono-, di-, or tri-substituted on the ring carbons with Y<sub>1</sub>, Y<sub>2</sub> and/or Y<sub>3</sub>,

(6) alkenyl of 2 to 6 carbon atoms which is optionally substituted with cycloalkyl of 3 to 8 carbon atoms, which is optionally mono-, di-, or tri-substituted on the ring carbons with Y<sub>1</sub>, Y<sub>2</sub> and/or Y<sub>3</sub>,

(7) aryl of 6 to 14 carbon atoms which is optionally mono-, di- or tri-substituted with Y<sub>1</sub>, Y<sub>2</sub> and/or Y<sub>3</sub>,

(8) heteroaryl of 5 to 14 ring atoms with the ring atoms selected from carbon and heteroatoms, wherein the heteroatoms are selected from oxygen, nitrogen, and sulfur, and which is optionally mono-, di-, or tri-substituted with Y<sub>1</sub>, Y<sub>2</sub> and/or Y<sub>3</sub>,

(9) aralkyl of 7 to 15 carbon atoms which is optionally substituted on the alkyl chain with hydroxy or halogen and which is optionally mono-, di-, or tri-substituted in the aryl ring with Y<sub>1</sub>, Y<sub>2</sub> and/or Y<sub>3</sub>,

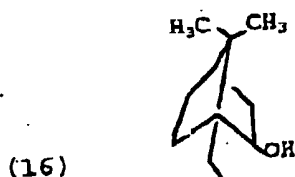
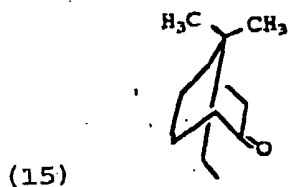
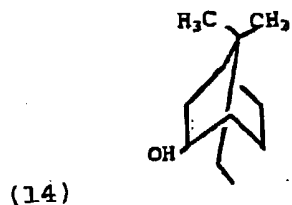
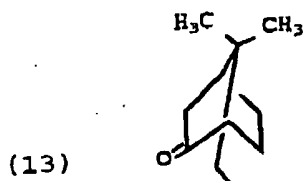
(10) heteroaralkyl of 5 to 14 ring atoms with the ring atoms selected from carbon and heteroatoms, wherein the heteroatoms are selected from oxygen, nitrogen, and sulfur, and which is optionally substituted on the alkyl chain with hydroxy or halogen and which is optionally mono-, di- or tri-substituted on the ring with Y<sub>1</sub>, Y<sub>2</sub> and/or Y<sub>3</sub>,

(11) aralkenyl of 8 to 16 carbon atoms which is optionally mono-, di-, or tri-substituted on the aryl ring with Y<sub>1</sub>, Y<sub>2</sub> and/or Y<sub>3</sub>,

(12) heteroaralkenyl of 5 to 14 ring atoms with the ring atoms selected from carbon and heteroatoms, wherein the heteroatoms are selected from oxygen, nitrogen, and sulfur, and

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which is optionally mono-, di- or tri-substituted on the ring with  $Y_1$ ,  $Y_2$  and/or  $Y_3$ .



(17) fused carbocyclic alkyl of 5 to 15 carbon atoms,

(18) difluoromethyl or perfluoroalkyl of 1 to 12 carbon atoms,

(19) perfluoroaryl of 6 to 14 carbon atoms,

(20) perfluoroalkyl of 7 to 15 carbon atoms, and

(21) hydrogen when X is a direct link;

wherein

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(i) each  $Y_1$ ,  $Y_2$  and  $Y_3$  is independently selected from the group consisting of halogen, cyano, nitro, tetrazolyl optionally substituted with alkyl of 1 to 6 carbon atoms, guanidino, amidino, methylamino, methylguanidino,  $-\text{CF}_3$ ,  $-\text{CF}_2\text{CF}_3$ ,  $-\text{CH}(\text{CF}_3)_2$ ,  $-\text{C}(\text{OH})(\text{CF}_3)_2$ ,  $-\text{OCF}_3$ ,  $-\text{OCF}_2\text{CF}_3$ ,  $-\text{OCF}_2\text{H}$ ,  $-\text{OC}(\text{O})\text{NH}_2$ ,  $-\text{OC}(\text{O})\text{NHZ}_1$ ,  $-\text{OC}(\text{O})\text{NZ}_1\text{Z}_2$ ,  $-\text{NHC}(\text{O})\text{Z}_1$ ,  $-\text{NHC}(\text{O})\text{NH}_2$ ,  $-\text{NHC}(\text{O})\text{NHZ}_1$ ,  $-\text{NHC}(\text{O})\text{NZ}_1\text{Z}_2$ ,  $-\text{C}(\text{O})\text{OH}$ ,  $-\text{C}(\text{O})\text{OZ}_1$ ,  $-\text{C}(\text{O})\text{NH}_2$ ,  $-\text{C}(\text{O})\text{NHZ}_1$ ,  $-\text{C}(\text{O})\text{NZ}_1\text{Z}_2$ ,  $-\text{P}(\text{O})_3\text{H}_2$ ,  $-\text{P}(\text{O})_3(\text{Z}_1)_2$ ,  $-\text{S}(\text{O})_3\text{H}$ ,  $-\text{S}(\text{O})_p\text{Z}_1$ ,  $-\text{Z}_1$ ,  $-\text{OZ}_1$ ,  $-\text{OH}$ ,  $-\text{NH}_2$ ,  $-\text{NHZ}_1$ ,  $-\text{NZ}_1\text{Z}_2$ , N-morpholino, and  $-\text{S}(\text{O})_p(\text{CF}_2)_q\text{CF}_3$ , wherein  $p$  is 0, 1 or 2,  $q$  is an integer from 0 to 5, and  $Z_1$  and  $Z_2$  are independently selected from the group consisting of alkyl of 1 to 12 carbon atoms, aryl of 6 to 14 carbon atoms, heteroaryl of 5 to 14 atoms having 1 to 9 carbon atoms, aralkyl of 7 to 15 carbon atoms, and heteroaralkyl of 5 to 14 ring atoms, or

(ii)  $Y_1$  and  $Y_2$  are selected together to be  $-\text{O}[\text{C}(\text{Z}_3)(\text{Z}_4)]_r\text{O}-$  or  $-\text{O}[\text{C}(\text{Z}_3)(\text{Z}_4)]_{r+1}-$ , wherein  $r$  is an integer from 1 to 4 and  $Z_3$  and  $Z_4$  are independently selected from the group consisting of hydrogen, alkyl or 1 to 12 carbon atoms, aryl of 6 to 14 carbon atoms, heteroaryl of 5 to 14 ring atoms having 1 to 9 carbon atoms, aralkyl of 7 to 15 carbon atoms, and heteroaralkyl of 5 to 14 ring atoms;

(c)  $Q$  is  $-\text{C}(\text{R}_4)-$ ;

(d)  $\text{R}_2$  is selected from the group consisting of hydrogen, halogen and alkyl of 1 to 6 carbon atoms;

(e)  $\text{R}_3$  is selected from the group consisting of hydrogen, alkyl 1 to 6 carbon atoms, cycloalkyl of 3 to 7 carbon atoms, alkoxy of 1 to 6 carbon atoms, halogen, and trifluoromethyl;

(f) alternatively,  $R_2$  and  $R_3$  are selected together and are  $-(CH_2)_k-$  where  $k$  is 3 or 4;

(g)  $R_4$  is selected from the group consisting of hydrogen, alkyl of 1 to 8 carbon atoms, hydroxy, alkoxy of 1 to 8 carbon atoms, aralkyl of 7 to 15 carbon atoms, alkyl of 1 to 5 carbon atoms substituted with cycloalkyl of 3 to 8 carbon atoms,  $-NHR_8$ ,  $-S(O)_tR_8$  and  $-C(=O)R_8$  where  $t$  is 0, 1 or 2;

(h)  $w$  is 0, 1 or 2;

(i)  $V$  is  $-CH(R_9)-$ ;

(j)  $R_5$  is hydrogen or alkyl of 1 to 6 carbon atoms;

(k)  $E$  is heteroaryl of 6 to 10 ring atoms having from 1 to 4 ring nitrogen atoms and the remainder of the ring atoms carbon atoms and which is substituted with  $R_6$  and  $R_7$ ;

(l)  $R_6$  and  $R_7$  are independently selected from the group consisting of hydrogen, halogen, hydroxy, alkyl of 1 to 6 carbon atoms, alkoxy of 1 to 6 carbon atoms, alkyl of 1 to 4 carbon atoms substituted with alkoxy of 1 to 4 carbon atoms, trifluoromethyl,  $-C(=O)OR_{10}$ ,  $-NHR_{10}$ ,  $-C(=O)R_{10}$ ,  $-C(=O)NHR_{10}$ ,  $-OC(=O)NHR_{10}$ ,  $-C(=NR_{10})NHR_{11}$ , and  $-N(R_{12})-C(=NR_{10})NHR_{11}$ ; and

(m)  $R_8$ ,  $R_9$ ,  $R_{10}$ ,  $R_{11}$  and  $R_{12}$  are independently selected from the group consisting of hydrogen, alkyl of 1 to 6 carbon atoms and  $-(CF_2)_jCF_3$  wherein  $j$  is 0, 1, 2 or 3; or pharmaceutically acceptable salts thereof.

2. (Cancelled)

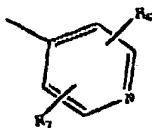
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~~2~~  
~~3.~~ (Previously presented) A compound according to claim 1 wherein  $R_9$  is hydrogen.

~~3~~  
~~4.~~ (Original) A compound according to claim 3 wherein X is  $-S(O)_2-$  or a direct link.

~~4~~  
~~5.~~ (Original) A compound according to claim 4 wherein  $R_1$  is substituted or unsubstituted aralkyl.

~~5~~  
~~6.~~ (Original) A compound according to claim 5 wherein E is



~~6~~  
~~7.~~ (Original) A compound according to claim 6 wherein  $R_6$  and  $R_7$  are independently hydrogen or halogen.

~~7~~  
~~8.~~ (Original) A compound according to claim 7 wherein at least one of  $R_6$  and  $R_7$  is hydrogen.

9. (Cancelled)

~~8~~  
10. (Previously presented) A compound according to claim 8 wherein w is 1.

~~9~~  
11. (Previously presented) A compound according to claim 8 wherein  $R_4$  is hydrogen.

~~10~~  
12. (Original) A compound according to claim 11 wherein w is 1.

13. (Cancelled)

~~11~~  
14. (Previously presented) A compound according to claim 1 wherein X is  $-S(O)_2-$ .

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12  
15. (Original) A compound according to claim 14 wherein  $R_9$  is hydrogen or methyl.

13  
16. (Cancelled)

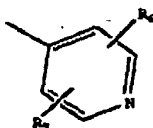
17. (Cancelled)

13  
18. (Previously presented) A compound according to claim 15 wherein  $R_1$  is substituted or unsubstituted aralkyl.

14  
19. (Original) A compound according to claim 18 wherein  $R_9$  is hydrogen.

15  
20. (Original) A compound according to claim 19 wherein  $w$  is 0 or 1.

16  
21. (Original) A compound according to claim 1 wherein  $E$  is



17  
22. (Original) A compound according to claim 21 wherein  $R_6$  and  $R_7$  are independently hydrogen or halogen.

18  
23. (Original) A compound according to claim 22 wherein at least one of  $R_6$  and  $R_7$  is hydrogen.

24. (Cancelled)

19  
25. (Previously presented) A compound according to claim 23 wherein  $R_9$  is hydrogen or methyl.

20  
26. (Previously presented) A compound according to claim 1 wherein  $X$  is  $-S(O_2)-$  or a direct link.

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21

27. (Original) A compound according to claim 26 wherein  $R_1$  is unsubstituted aralkyl, substituted aralkyl or alkyl substituted with cycloalkyl in which the cycloalkyl group is substituted with aryl or heteroaryl.

22

28. (Original) A compound according to claim 27 wherein  $R_2$  is hydrogen and  $R_3$  is hydrogen or methyl.

23

29. (Original) A compound according to claim 28 wherein  $R_3$  is methyl.

Claims 30 to 32 (Cancelled)

24

33. (Previously presented) A compound according to claim 1 selected from the group consisting of Compounds A, E, F, G, H, I, J, K, L, M, N, P, Q and R depicted in Figures 1A and 1B.

25

34. (Currently amended) A pharmaceutical composition ~~for treating or decreasing the incidence of a condition in a mammal characterized by abnormal thrombosis,~~ comprising a therapeutically pharmaceutically acceptable carrier, and a therapeutically effective amount of compound of claim 1.

26

35. (Currently amended) A pharmaceutical composition ~~for treating or decreasing the incidence of a condition in a mammal characterized by abnormal thrombosis,~~ comprising a therapeutically pharmaceutically acceptable carrier, and a therapeutically effective amount of compound of claim 3.

27

36. (Currently amended) A pharmaceutical composition ~~for treating or decreasing the incidence of a condition in a mammal characterized by abnormal thrombosis,~~ comprising a therapeutically pharmaceutically acceptable carrier, and a therapeutically effective amount of compound of claim 6.

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37. (Currently amended) A pharmaceutical composition for ~~treating or decreasing the incidence of a condition in a mammal characterized by abnormal thrombosis,~~ comprising a therapeutically pharmaceutically acceptable carrier, and a therapeutically effective amount of compound of claim 15.

29

38. (Currently amended) A pharmaceutical composition for ~~treating or decreasing the incidence of a condition in a mammal characterized by abnormal thrombosis,~~ comprising a therapeutically pharmaceutically acceptable carrier, and a therapeutically effective amount of compound of claim 19.

46

39. (Amended) (Currently amended) A pharmaceutical composition ~~for treating or decreasing the incidence of a condition in a mammal characterized by abnormal thrombosis,~~ comprising a therapeutically pharmaceutically acceptable carrier, and a therapeutically effective amount of compound of claim 53.<sup>40</sup>

47

40. (Amended) (Currently amended) A pharmaceutical composition ~~for treating or decreasing the incidence of a condition in a mammal characterized by abnormal thrombosis,~~ comprising a therapeutically pharmaceutically acceptable carrier, and a therapeutically effective amount of compound of claim 55.<sup>42</sup>

30

41. (Currently amended) A pharmaceutical composition for ~~treating or decreasing the incidence of a condition in a mammal characterized by abnormal thrombosis,~~ comprising a therapeutically pharmaceutically acceptable carrier, and a therapeutically effective amount of compound of claim 33.

31  
42. (Currently amended) A method for treating or ~~decreasing the incidence of~~ a condition in a mammal characterized by ~~abnormal~~ thrombosis, comprising administering to said mammal a therapeutically effective amount of the compound of claim 1.

32  
43. (Currently amended) A method for treating or ~~decreasing the incidence of~~ a condition in a mammal characterized by ~~abnormal~~ thrombosis, comprising administering to said mammal a therapeutically effective amount of the compound of claim 3.

33  
44. (Currently amended) A method for treating or ~~decreasing the incidence of~~ a condition in a mammal characterized by ~~abnormal~~ thrombosis, comprising administering to said mammal a therapeutically effective amount of the compound of claim 6.

34  
45. (Currently amended) A method for treating or ~~decreasing the incidence of~~ a condition in a mammal characterized by ~~abnormal~~ thrombosis, comprising administering to said mammal a therapeutically effective amount of the compound of claim 15.

35  
46. (Currently amended) A method for treating or ~~decreasing the incidence of~~ a condition in a mammal characterized by ~~abnormal~~ thrombosis, comprising administering to said mammal a therapeutically effective amount of the compound of claim 19.

48  
47. (Amended) (Currently amended) A method for treating or ~~decreasing the incidence of~~ a condition in a mammal characterized by ~~abnormal~~ thrombosis, comprising administering

to said mammal a therapeutically effective amount of the compound of claim 53.<sup>40</sup>

<sup>49</sup>  
~~48.~~ (Currently amended) A method for treating ~~or~~  
~~decreasing the incidence of~~ a condition in a mammal  
characterized by ~~abnormal~~ thrombosis, comprising administering  
to said mammal a therapeutically effective amount of the  
compound of claim 55.<sup>40</sup>

<sup>36</sup>  
~~48.~~ (Currently amended) A method for treating ~~or~~  
~~decreasing the incidence of~~ a condition in a mammal  
characterized by ~~abnormal~~ thrombosis, comprising administering  
to said mammal a therapeutically effective amount of the  
compound of claim 33.

<sup>37</sup>  
~~50.~~ (Previously presented) A compound according to claim  
15 wherein R<sub>4</sub> is hydrogen.

<sup>38</sup>  
<sup>37</sup>  
~~50~~ ~~51.~~ (Previously presented) A compound according to claim  
50 wherein R<sub>2</sub> is hydrogen.

<sup>39</sup>  
<sup>38</sup>  
~~51~~ ~~52.~~ (Previously presented) A compound according to claim  
51 wherein R<sub>3</sub> is methyl.

<sup>40</sup>  
~~53.~~ (Previously presented) A compound according to claim  
29 wherein R<sub>4</sub> is hydrogen.

<sup>41</sup>  
~~54.~~ (Previously presented) A compound according to claim 1  
wherein R<sub>4</sub> is hydrogen.

<sup>42</sup>  
<sup>41</sup>  
~~54~~ ~~55.~~ (Previously presented) A compound according to claim  
54 wherein R<sub>2</sub> is hydrogen.

<sup>43</sup>  
<sup>42</sup>  
~~55~~ ~~56.~~ (Previously presented) A compound according to claim  
55 wherein R<sub>3</sub> is methyl.

<sup>44</sup>  
57. (Previously presented) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of any of claims 1, 3, 6, 15, 19, 33, <sup>40</sup>53 or <sup>42</sup>55.

<sup>45</sup>  
58. (Currently amended) A method of ~~preventing or~~ treating in a mammal a condition of ~~abnormal~~ thrombus formation which comprises administering to said mammal a therapeutically effective amount of a compound of any of claims 1, 3, 6, 15, 19, 33, <sup>40</sup>53 or <sup>42</sup>55.

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